

Application No. 10/743,281
Amendment and Response dated May 5, 2007

BHGL Ref. 10709/63

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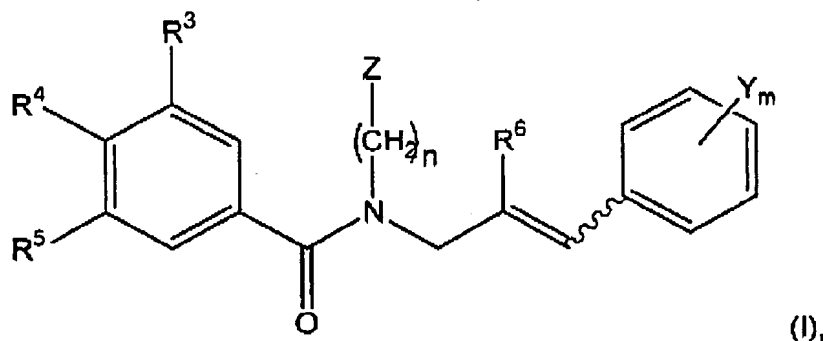
Amendments to the Claims:

Please amend claim 19 as follows:

A complete listing of the claims is listed below with the proper claim identifiers;
this listing of claims will replace all prior versions, and listings, of claims in the
application:

What is claimed is:

1. (Original) A modulator of the structure (I), or a salt thereof:



where m is an integer from 1 to 5;

each Y is independently selected from the group consisting of hydrogen, halogen, -CN, -NO₂, -OH, -OR', -C(O)R', -CO₂R', -O(CO)R', -C(O)NR'R'', -OC(O)NR'R'', -SR', -SOR', -SO₂R', -SO₂NR'R'', -NR'R'', -NR'C(O)R'', -NR'C(O)₂R'', -NR'SO₂R'', -NR'(CO)NR'R'', unsubstituted or substituted C₁₋₈ alkyl, unsubstituted or substituted C₂₋₈ alkenyl, unsubstituted or substituted C₂₋₈ alkynyl, unsubstituted or substituted C₃₋₈ cycloalkyl, unsubstituted or substituted C₆₋₁₀ aryl, unsubstituted or substituted 5- to 10-membered heteroaryl, and unsubstituted or substituted 3- to 10-membered heterocyclyl;

where each R', R'' and R''' are independently hydrogen, halogen, unsubstituted or substituted C₁₋₈ alkyl, unsubstituted or substituted C₆₋₁₀ aryl, unsubstituted or substituted 5- to 10-membered heteroaryl, and unsubstituted or substituted 3- to 10-membered heterocyclyl;

n is 0, 1, 2 or 3;

Z is -CHR¹R²-, -OR¹, or -NR¹R²;

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R¹ and R² are each independently substituted or unsubstituted alkyl or hydrogen, or Z in combination with R¹ and R² form a substituted or unsubstituted 5- to 8-membered ring comprising at least one nitrogen and 0 to 3 additional heteroatoms;

R⁶ is alkyl, hydrogen, or halogen; and

R³, R⁴, and R⁵ are each independently selected from the group consisting of hydrogen, halogen, -CN, -NO₂, -OH, -OR', -C(O)R', -CO₂R', -O(CO)R', -C(O)NR'R'', -OC(O)NR'R'', -SR', -SOR', -SO₂R', -SO₂NR'R'', -NR'R'', -NR'C(O)R'', -NR'C(O)₂R'', -NR'SO₂R'', -NR'(CO)NR'R'', unsubstituted or substituted C₁₋₈ alkyl, unsubstituted or substituted C₂₋₈ alkenyl, unsubstituted or substituted C₂₋₈ alkynyl, unsubstituted or substituted C₃₋₈ cycloalkyl, unsubstituted or substituted C₈₋₁₀ aryl, unsubstituted or substituted 5- to 10-membered heteroaryl, and unsubstituted or substituted 3- to 10-membered heterocyclyl, or where any two of R³, R⁴ or R⁵ together with the atoms which they substituted form a substituted or unsubstituted 3- to 10-membered heterocycl.

2. (Original) The modulator of claim 1, where R⁶ is hydrogen.
3. (Original) The modulator of claim 1, where R⁶ is substituted or unsubstituted C₁₋₈ alkyl.
4. (Original) The modulator of claim 1, where R⁶ is halogen.
5. (Original) The modulator of claim 1, where R³, R⁴, and R⁵ are each independently selected from the group consisting of hydrogen, -OR', and substituted or unsubstituted C₁₋₈ alkyl.
6. (Original) The modulator of claim 1, where R³, R⁴, and R⁵ are each independently selected from the group consisting of -OR' and hydrogen.
7. (Original) The modulator of claim 1, where R³, R⁴, and R⁵ are each -OR', where R' is substituted C₁₋₈ alkyl.
8. (Original) The modulator of claim 1, where R⁴ and R⁵ together with the atom which they substitute form substituted or unsubstituted 5- to 6-membered heterocyclyl containing 1 to 2 oxygen atoms.
9. (Original) The modulator of claim 1, where Z is CHR¹R² and where R¹ and R² together with Z form C₃₋₁₀ cycloalkyl with 0 to 3 substituents selected from the group

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consisting of halogen, -CN, -NO₂, -OH, -OR', -C(O)R', -CO₂R', -O(CO)R', -C(O)NR'R'', -OC(O)NR'R'', -SR', -SOR', -SO₂R', -SO₂NR'R'', -NR'R'', -NR'C(O)R'', -NR'C(O)₂R'', -NR'SO₂R'', -NR'(CO)NR'R'', unsubstituted or substituted C₁₋₈ alkyl, unsubstituted or substituted C₂₋₈ alkenyl, unsubstituted or substituted C₂₋₈ alkynyl, unsubstituted or substituted C₃₋₈ cycloalkyl, unsubstituted or substituted C₆₋₁₀ aryl, unsubstituted or substituted 5- to 10-membered heteroaryl, and unsubstituted or substituted 3- to 10-membered heterocyclyl.

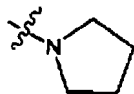
10. (Original) The modulator of claim 1, where R¹ and R² together with Z form a 3- to 10-membered heterocyclyl with 0 to 3 substituents selected from the group consisting of halogen, -OR, substituted or unsubstituted C₁₋₈ alkyl, substituted or unsubstituted C₁₋₈ alkenyl, substituted or unsubstituted C₁₋₈ alkynyl, substituted or unsubstituted C₆₋₁₀ aryl, substituted or unsubstituted 5- to 10-membered heteroaryl.

11. (Original) The modulator of claim 1, where Z is -CHR¹R²-.

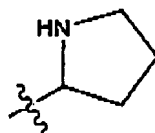
12. (Original) The modulator of claim 1, where Z is -N R¹R²-.

13. (Original) The modulator of claim 1, where Z in combination with R¹ and R² is selected from the group consisting of substituted or unsubstituted morpholinyl, substituted or unsubstituted pyrrolidinyl, substituted or unsubstituted piperidinyl, and substituted or unsubstituted piperazinyl.

14. (Original) The modulator of claim 1, where Z is a substituted or unsubstituted group of the formula:



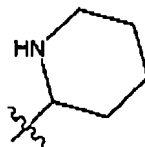
15. (Original) The modulator of claim 1, where Z is a substituted or unsubstituted group of the formula:



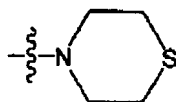
16. (Original) The modulator of claim 1, where Z is a substituted or unsubstituted group of the formula:

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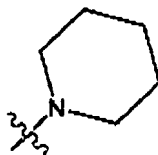
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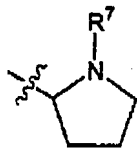
17. (Original) The modulator of claim 1, where Z is a substituted or unsubstituted group of the formula:



18. (Original) The modulator of claim 1, where Z is a substituted or unsubstituted group of the formula:



19. (Currently Amended) The modulator of claim 1, where Z is a substituted or unsubstituted group of the formula:



where R^7 is selected from the group consisting of hydrogen, $-C(O)R'$, $-CO_2R'$, $-C(O)NR'R''$, $-SO_2R'$, unsubstituted or substituted C_{1-10} alkyl, unsubstituted or substituted C_{1-8} alkoxy, unsubstituted or substituted C_{2-10} alkenyl, unsubstituted or substituted C_{2-10} alkynyl, unsubstituted or substituted C_{3-10} cycloalkyl, unsubstituted or substituted C_{6-10} aryl, C_{6-10} aryloxy unsubstituted or substituted 5- to 10-membered heteroaryl, and unsubstituted or substituted 3- to 10-membered heterocyclyl.

20. (Original) The modulator of claim 1, where R^7 is substituted or unsubstituted C_{1-10} alkyl, substituted or unsubstituted C_{1-10} alkoxy, substituted or unsubstituted aryloxy, or substituted or unsubstituted C_{3-10} cycloalkyl.
21. (Original) The modulator of claim 1, where n is 1, 2, or 3.

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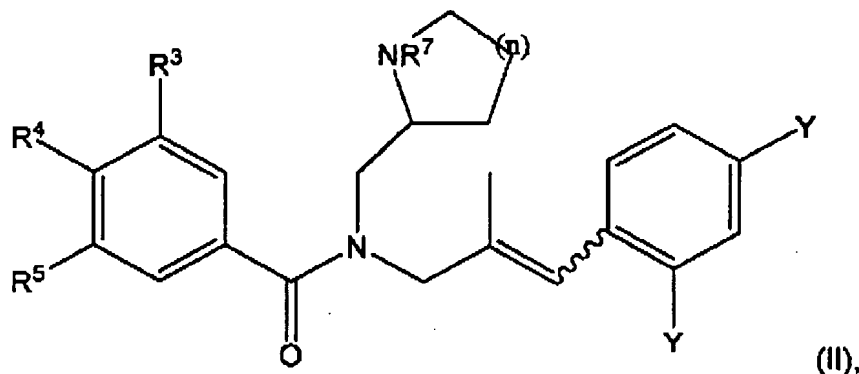
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22. (Original) The modulator of claim 1, where m is 1 or 2, and each Y is a halogen.
23. (Original) The modulator of claim 1, where m is 0.
24. (Original) The modulator of claim 1, where substituted alkyl, substituted alkenyl, substituted alkynyl and substituted cycloalkyl can each independently be substituted 1 to 3 times with halogen, -OR', -NR'R'', -SR', -SiR'R''R'', -OC(O)R', -C(O)R', -CO₂R', -CONR'R'', -OC(O)NR'R'', -NR''C(O)R', -NR'-C(O)NR''R'', -NR''C(O)₂R', -S(O)R', -S(O)₂R', -S(O)₂NR'R'', -NR'S(O)₂R'', -CN, oxo (=O or -O-) or -NO₂, where R', R'' and R''' each independently hydrogen, halogen, unsubstituted C₁₋₈ alkyl, unsubstituted C₃₋₈ cycloalkyl, unsubstituted C₂₋₈ alkenyl, unsubstituted or C₂₋₈ alkynyl, unsubstituted aryl, unsubstituted heteroaryl, unsubstituted or substituted heterocyclyl.
25. (Original) The modulator of claim 1, where substituted aryl and substituted heteroaryl can each independently be substituted 1 to 3 times with halogen, unsubstituted or substituted alkyl, unsubstituted or substituted alkenyl, unsubstituted or substituted alkynyl, unsubstituted or substituted cycloalkyl, -OR', oxo (=O or -O), -OC(O)R', -NR'R'', -SR', -R', -CN, -NO₂, -CO₂R', -CONR'R'', -C(O)R', -OC(O)NR'R'', -NR''C(O)R', -NR''C(O)₂R', -NR'-C(O)NR''R'', -NH-C(NH₂)=NH, -NR'C(NH₂)=NH, -NH-C(NH₂)=NR', -S(O)R', -S(O)₂R', -S(O)₂NR'R'', -NR'S(O)₂R'' and -N₃, where R', R'' and R''' each independently hydrogen, halogen, unsubstituted C₁₋₈ alkyl, unsubstituted C₃₋₈ cycloalkyl, unsubstituted C₂₋₈ alkenyl, unsubstituted C₂₋₈ alkynyl, unsubstituted or substituted aryl, unsubstituted heteroaryl, unsubstituted heterocyclyl.
26. (Original) The modulator of claim 1, where substituted heterocyclyl can be substituted 1 to 3 times with halogen, unsubstituted or substituted alkyl, unsubstituted or substituted alkenyl, unsubstituted or substituted alkynyl, unsubstituted or substituted cycloalkyl, -OR', oxo (=O or -O), -OC(O)R', -NR'R'', -SR', -R', -CN, -NO₂, -OC(O)NR'R'', -NR''C(O)R', -NR''C(O)₂R', -NR'-C(O)NR''R'', -NH-C(NH₂)=NH, -NR'C(NH₂)=NH, -NH-C(NH₂)=NR', -S(O)R', -S(O)₂NR'R'', -NR'S(O)₂R'' and -N₃, where R', R'' and R''' each independently hydrogen, halogen, unsubstituted C₁₋₈ alkyl, unsubstituted or C₃₋₈ cycloalkyl, unsubstituted C₂₋₈ alkenyl, unsubstituted C₂₋₈ alkynyl, unsubstituted aryl, unsubstituted heteroaryl, unsubstituted heterocyclyl.

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27. (Original) A modulator having the structure (II):



where $n=0-4$

where each Y is independently hydrogen or halogen;

R^3 , R^4 , and R^5 are each independently R^3 , R^4 , and R^5 are each independently selected from the group consisting of hydrogen, halogen, and $-OR^1$;

or any two of R^3 , R^4 , and R^5 , together with the atoms which they substituted, form unsubstituted or substituted 3- to 10-membered heterocyclyl; and

R^7 is selected from the group consisting of hydrogen, $-C(O)R^1$, $-CO_2R^1$, $-C(O)NR^1R^2$, $-SO_2R^1$, unsubstituted or substituted C_{1-8} alkyl (optionally C_{1-8} alkoxyalkoxy, $CH_2CH_2OCH_2CH_2OMe$)alkyl, unsubstituted or substituted C_{2-8} alkenyl, unsubstituted or substituted C_{2-8} alkynyl, unsubstituted or substituted C_{3-8} cycloalkyl, unsubstituted or substituted C_{6-10} aryl, unsubstituted or substituted 5- to 10-membered heteroaryl, and unsubstituted or substituted 3- to 10-membered heterocyclyl.

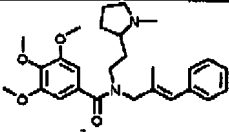
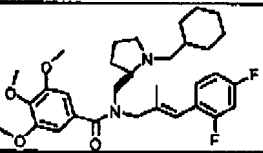
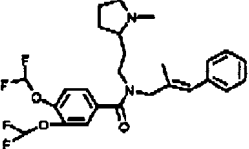
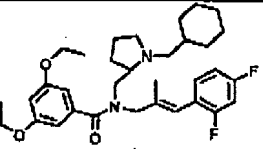
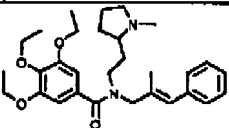
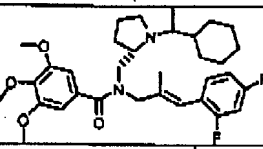
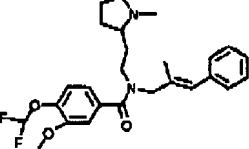
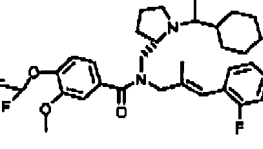
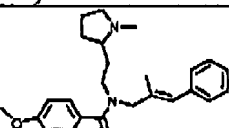
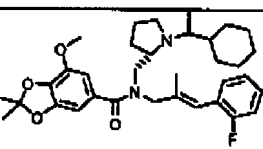
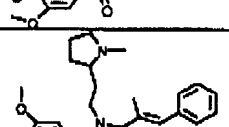
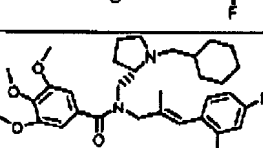
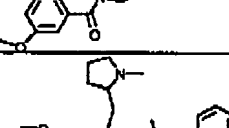
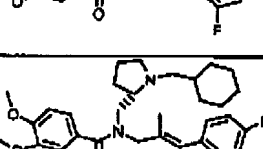
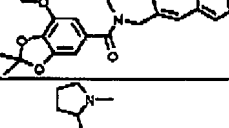
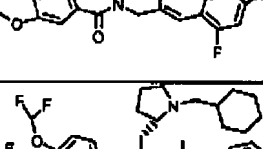
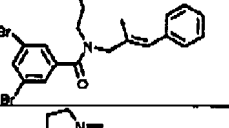
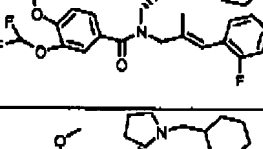
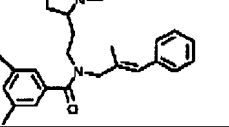
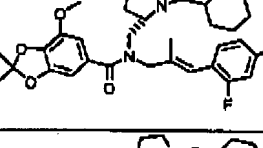
28. (Original) The modulator of claim 27, where R^7 is C_{1-8} alkoxyalkoxy.

29. (Original) The modulator of claim 27, where n is 1.

30. (Original) A modulator comprising one of the following formulae:

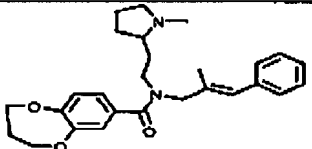
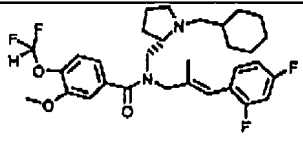
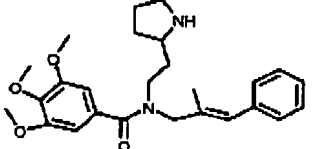
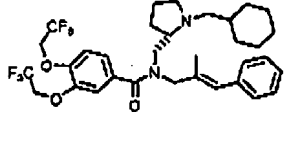
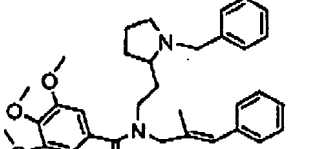
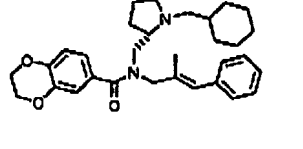
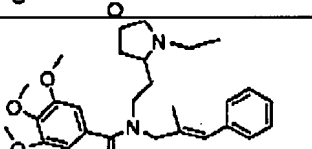
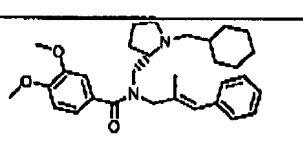
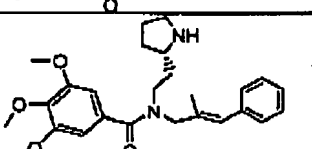
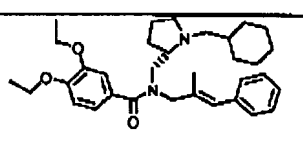
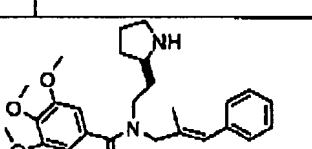
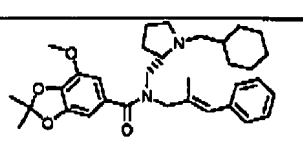
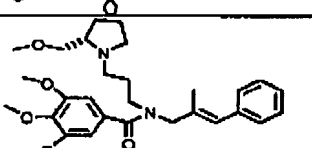
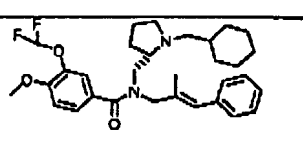
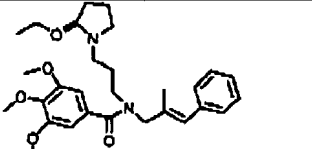
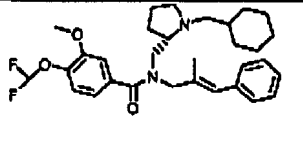
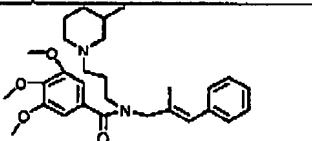
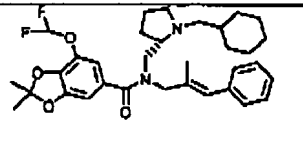
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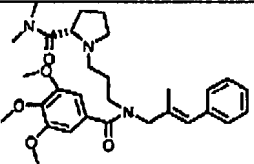
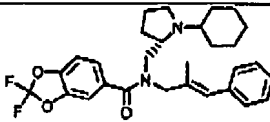
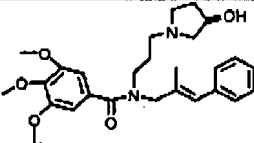
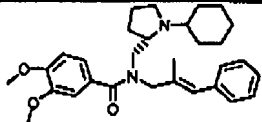
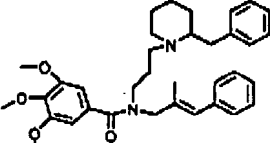
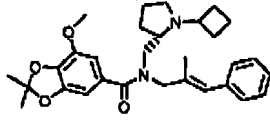
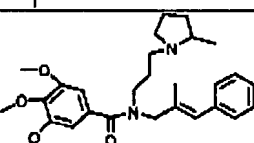
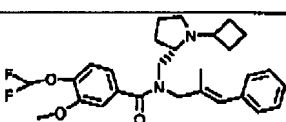
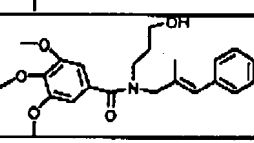
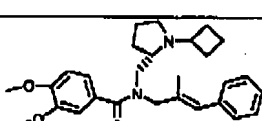
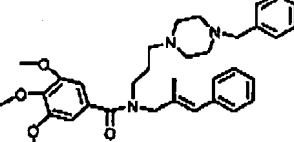
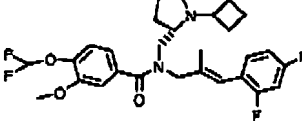
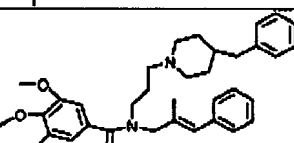
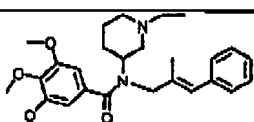
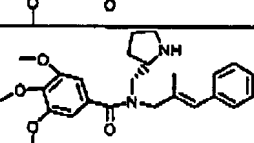
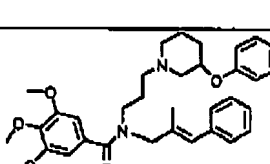
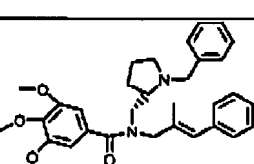
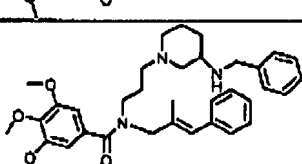
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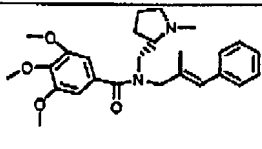
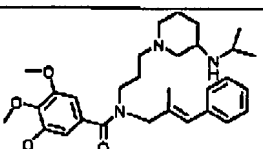
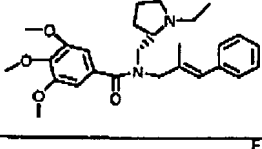
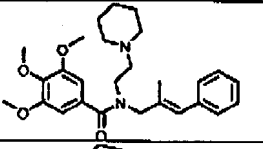
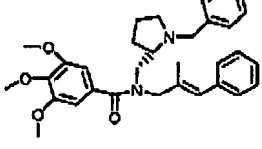
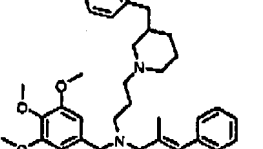
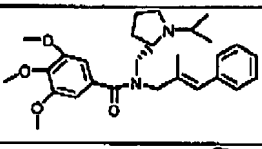
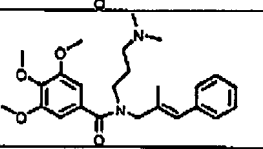
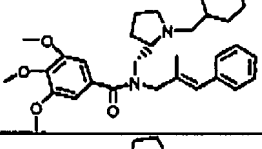
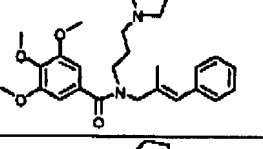
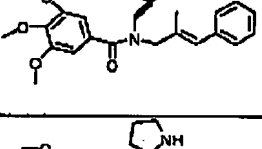
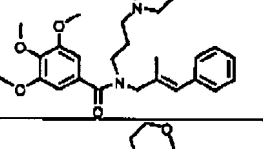
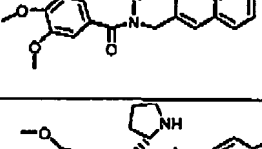
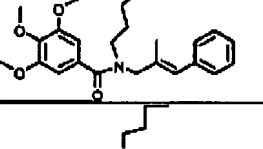
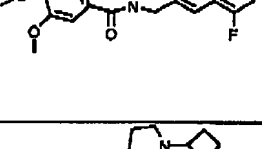
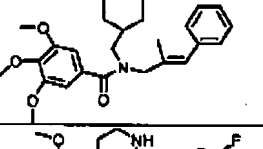
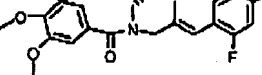
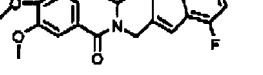
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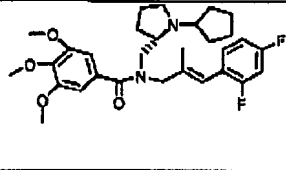
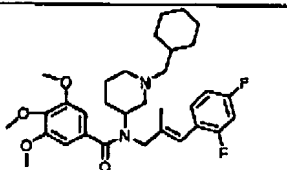
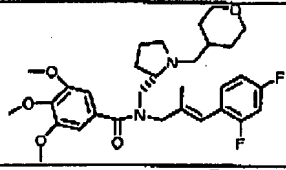
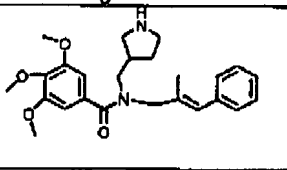
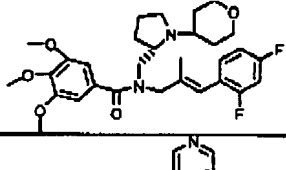
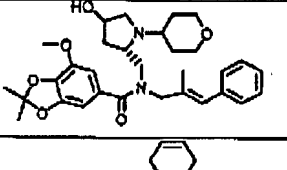
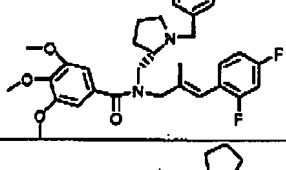
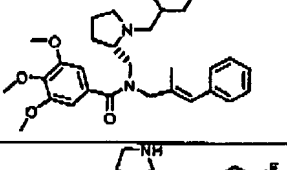
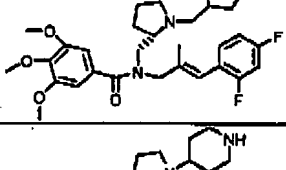
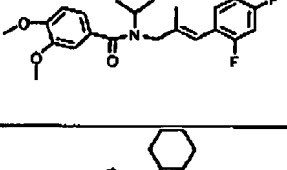
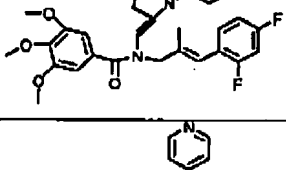
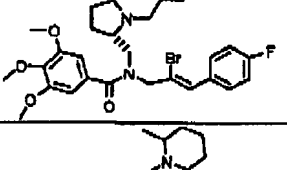
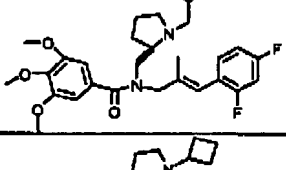
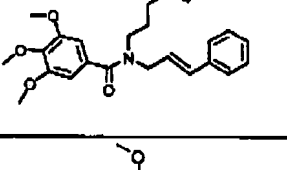
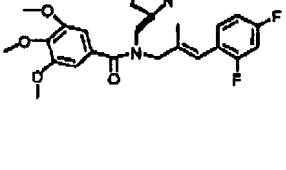
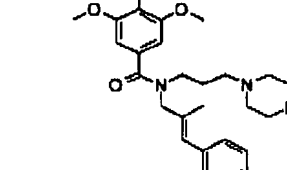
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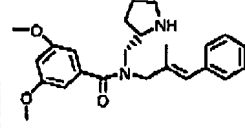
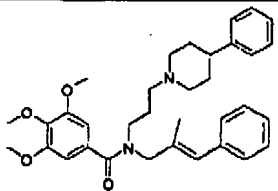
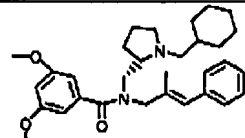
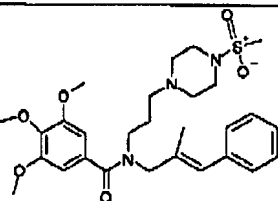
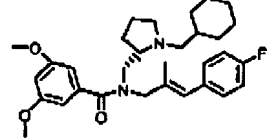
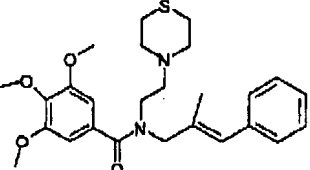
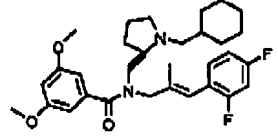
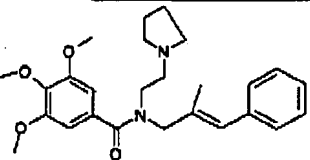
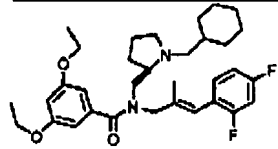
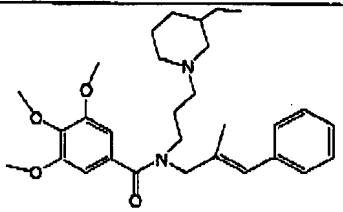
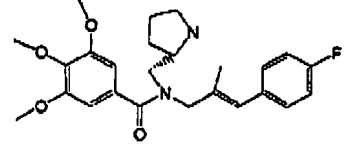
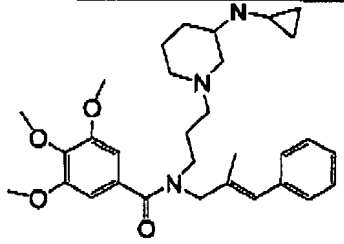
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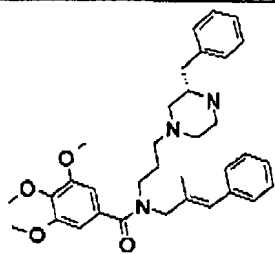
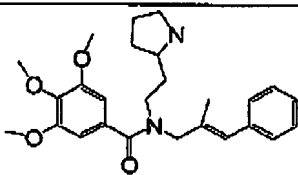
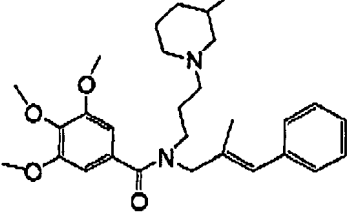
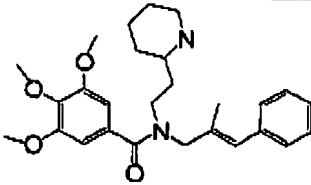
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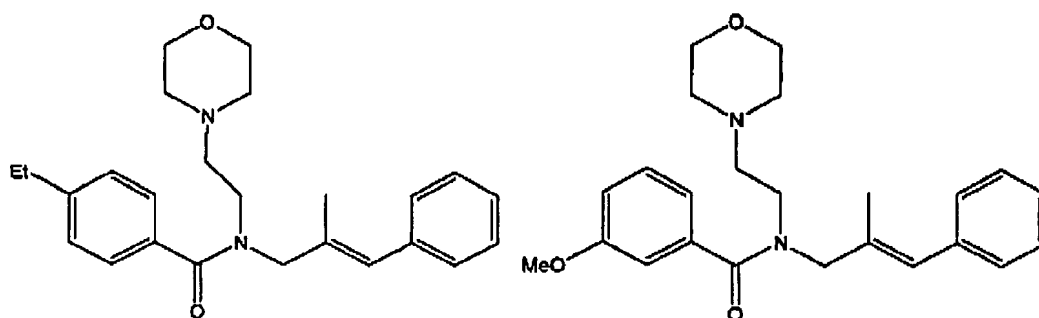
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31. (Original) A pharmaceutical composition comprising the modulator of claim 1 and a pharmaceutically acceptable carrier.

32. (Original) A pharmaceutical composition comprising the modulator of claim 27 and a pharmaceutically acceptable carrier.

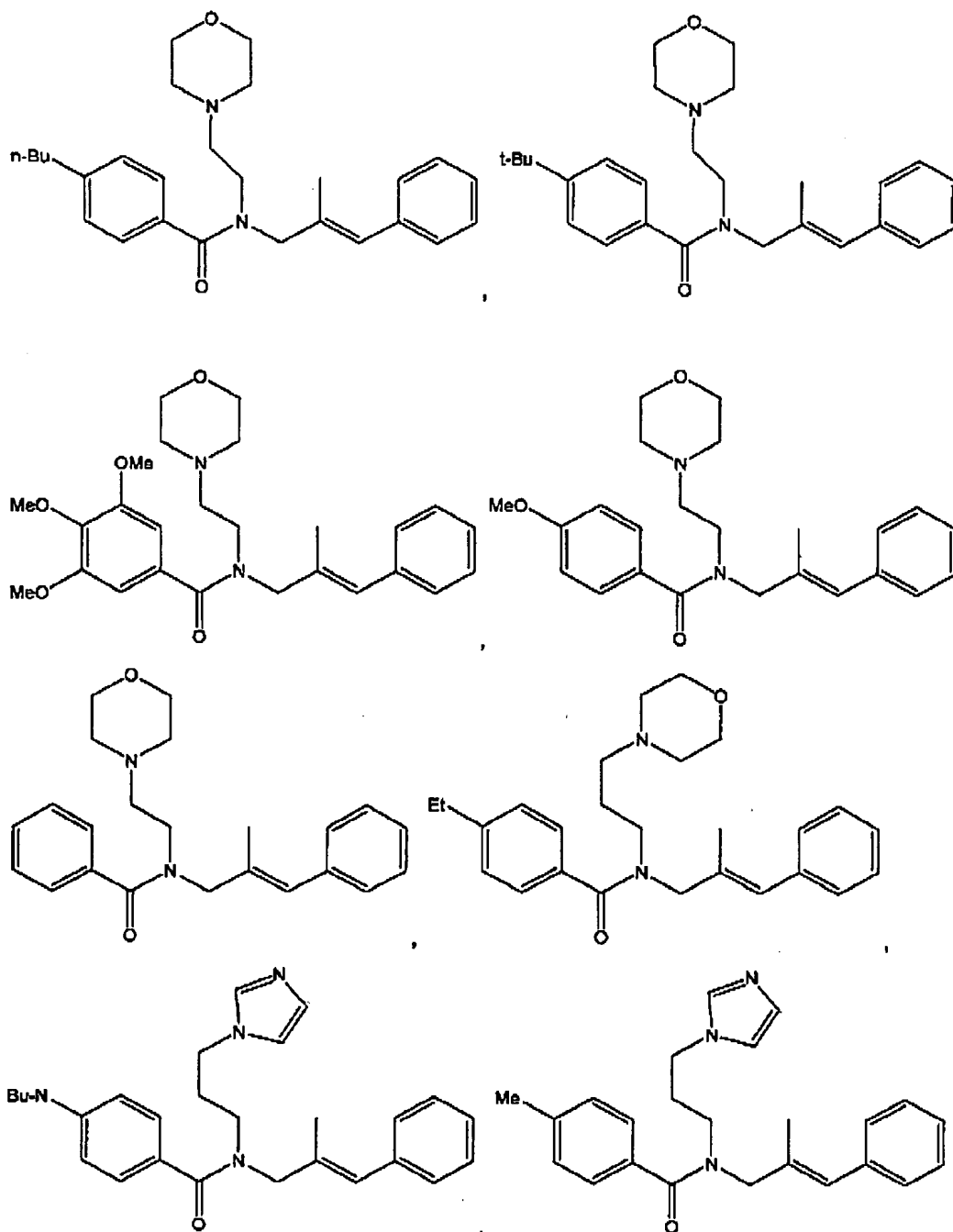
33. (Previously presented) A pharmaceutical composition comprising the modulator of claim 30 and a pharmaceutically acceptable carrier.

34. (Original) A pharmaceutical composition comprising a compound of the formulae:



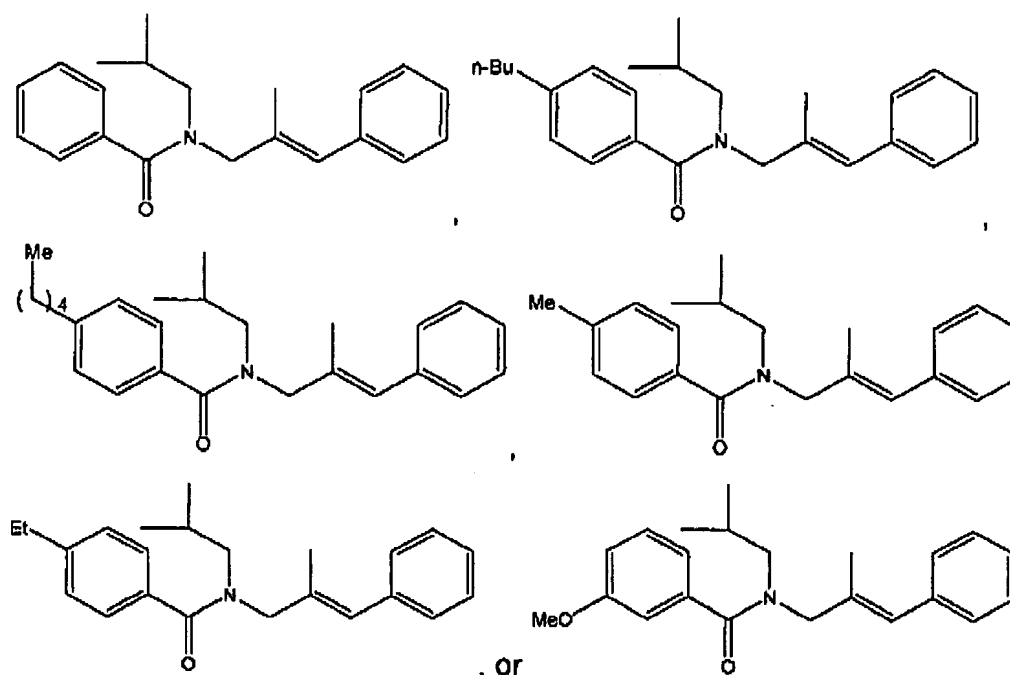
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and a pharmaceutically acceptable carrier.

35. (Previously presented) A method of inhibiting the binding of chemokines I-TAC and/or SDF-1 to a CCXCR2 receptor, comprising contacting the composition of claim 34 with a cell that expresses the CCXCR2 receptor for a time sufficient to inhibit the binding of the chemokines to the CCXCR2 receptor.

36. (Original) A method of inhibiting the binding of chemokines I-TAC and/or SDF-1 to a CCXCR2 receptor, comprising contacting the modulator of claim 1 with a cell that expresses the CCXCR2 receptor for a time sufficient to inhibit the binding of the chemokines to the CCXCR2 receptor.

37. (Previously presented) A method of treating cancer, comprising administering a therapeutically effective amount of the composition of claim 34 to a cancer patient for a time sufficient to treat the cancer.

38. (Original) A method of treating cancer, comprising administering a therapeutically effective amount of the modulator of claim 1 to a cancer patient for a time sufficient to treat the cancer.